IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Ian Alexander Shiels and David Fairlie	Confirmation No. 3534
Application Number: 10/531,560	Group Art Unit: 1654
Filing Date: January 27, 2006	Examiner: Khanna, Hemant
For: TREATMENT OF OSTEOARTHRITIS	Attorney Docket No.: **36677.32**

1. AMENDMENT; 2. RESPONSE TO SPECIES ELECTION REQUIREMENT DATED AUGUST 23, 2006

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The Examiner is respectfully requested to enter the following amendment. A response to the Official Action (Species Election) dated August 23, 2006 ("the Action"), is also submitted, and the Examiner is requested to consider the remarks and enter the election therein. Applicants believe that the present materials place the claims in condition for initial examination on the merits and consideration of the amendment and remarks herein is respectfully requested.

A Petition for an Extension of Time of Four Months to and including January 23, 2006, is included herewith to render the amendment and response timely submitted. Should any additional fees be deemed necessary for any reason in connection with the present submission, the Commissioner is hereby authorized to deduct any necessary amounts from Deposit Account No. 08-1394, Order No. 38871.32.

1. LISTING OF THE CLAIMS:

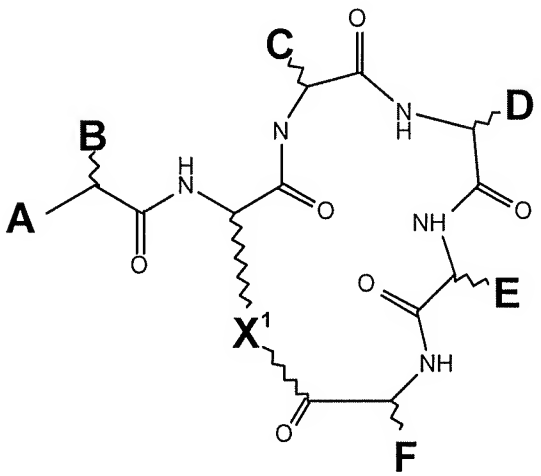
This listing of claims will replace all prior versions and listings of claims in the application:

1. (Original) A method of treatment of osteoarthritis, comprising the step of administering an effective amount of an inhibitor of a G protein-coupled receptor to a subject in need of such treatment, in which the inhibitor is a compound which

(a) is an antagonist of a G protein-coupled receptor,

(b) has substantially no agonist activity, and

(c) is a cyclic peptide or peptidomimetic compound of formula I



where **A** is H, alkyl, aryl, NH_2, NH-alkyl, $N(alkyl)_2$, NH-aryl, NH-acyl, NH-benzoyl, $NHSO_3$, $NHSO_2$-alkyl, $NHSO_2$-aryl, OH, O-alkyl, or O-aryl;

B is an alkyl, aryl, phenyl, benzyl, naphthyl or indole group, or the side chain of a D- or L-amino acid, but is not the side chain of glycine, D-phenylalanine, L-homophenylalanine, L-tryptophan, L-homotryptophan, L-tyrosine, or L-homotyrosine;

C is the side chain of a D-, L- or homo-amino acid, but is not the side chain of isoleucine, phenylalanine, or cyclohexylalanine;

D is the side chain of a neutral D-amino acid, but is not the side chain of glycine or D-alanine, a bulky planar side chain, or a bulky charged side chain;

E is a bulky substituent, but is not the side chain of D-tryptophan, L-*N*-methyltryptophan, L-homophenylalanine, L-2-naphthyl L-tetrahydroisoquinoline, L-cyclohexylalanine, D-leucine, L-fluorenylalanine, or L-histidine;

F is the side chain of L-arginine, L-homoarginine, L-citrulline, or L-canavanine, or a bioisostere thereof; and

$\mathbf{X^1}$ is $-(CH_2)_nNH-$ or $(CH_2)_nS-$, where n is an integer of from 1 to 4; $-(CH_2)_2O-$; $-(CH_2)_3O-$; $-(CH_2)_3-$; $-(CH_2)_4-$; $-CH_2COCHRNH-$; or $-CH_2.CHCOCHRNH-$, where R is the side chain of any common or uncommon amino acid.

2. (Currently Amended) ~~A method according to~~The method of claim 1, in which *n* is 2 or 3.

3. (Currently Amended) ~~A method according to~~The method of claim 1, in which **A** is an acetamide group, an aminomethyl group, or a substituted or unsubstituted sulphonamide group.

4. (Currently Amended) ~~A method according to~~The method of claim 2, in which **A** is a substituted sulphonamide, and the substituent is an alkyl chain of 1 to 6 carbon atoms, or a phenyl or toluyl group.

5. (Currently Amended) ~~A method according to~~The method of claim 3, in which the substituent is an alkyl chain of 1 to 4 carbon atoms.

6. (Currently Amended) ~~A method according to~~The method of claim 1, in which **B** is the side chain of L-phenylalanine or L-phenylglycine.

7. (Currently Amended) ~~A method according to~~The method of claim 1, in which **C** is the side chain of glycine, alanine, leucine, valine, proline, hydroxyproline, or thioproline.

8. (Currently Amended) ~~A method according to~~The method of claim 1, in which **D** is the side chain of D-leucine, D-homoleucine, D-cyclohexylalanine, D-homocyclohexylalanine, D-valine, D-norleucine, D-homo-norleucine, D-phenylalanine, D-tetrahydroisoquinoline, D-glutamine, D-glutamate, or D-tyrosine.

9. (Currently Amended) ~~A method according to~~The method of claim 1, in which **E** is the side chain of an amino acid selected from the group consisting of L-phenylalanine, L-tryptophan and L-homotryptophan, or is L-1-napthyl or L-3-benzothienyl alanine.

10. (Currently Amended) ~~A method according to~~The method of claim 1, in which the inhibitor is a compound which has antagonist activity against C5aR, and has no C5a agonist activity.

11. (Currently Amended) ~~A method according to~~The method of claim 1, in which the inhibitor has potent antagonist activity at sub-micromolar concentrations.

12. (Currently Amended) ~~A method according to~~The method of claim 1, in which the compound has a receptor affinity $IC_{50} < 25$ μM, and an antagonist potency $IC_{50} < 1$ μM.

13. (Currently Amended) ~~A method according to~~The method of claim 1, in which the compound is selected from the group consisting of compounds **1** to **6**, **10** to **15**, **17**, **19**, **20**, **22**, **25**, **26**, **28**, **30**, **31**, **33** to **37**, **39** to **45**, **47** to **50**, **52** to **58** and **60** to **70** described in PCT/AU02/01427.

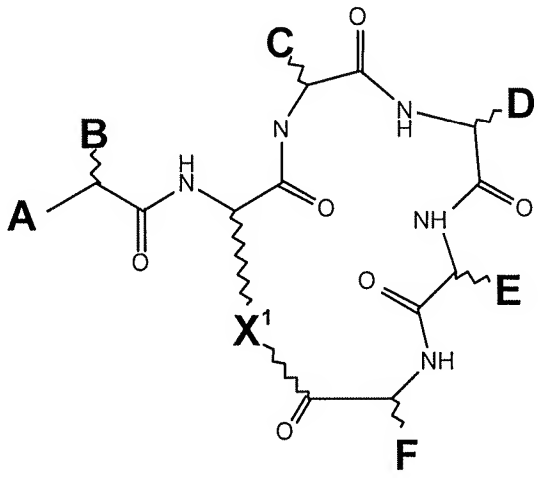
14. (Currently Amended) ~~A method according to~~The method of claim 13, in which the compound is compound **1** (AcF-[OP-DCha-WR]), compound **33** (AcF-[OP-DPhe-WR]), compound **60** (AcF-[OP-DCha-FR]) or compound **45** (AcF-[OP-DCha-WCit]) described in PCT/AU02/01427.

15. (Currently Amended) ~~A method according to~~The method of claim 1, in which the inhibitor is used in conjunction with one or more other agents for the treatment of osteoarthritis.

16. (New) The method of claim 1, wherein **A** is NH-acyl; **B** is the side chain of L-phenylalanine; **C** is the side chain of L-proline; **D** is the side chain of

D-cyclohexylalanine; **E** is the side chain of L-tryptophan; **F** is the side chain of L-arginine; and $\mathbf{X^1}$ is $-(CH_2)_nNH-$, where n is 3.

17. (New) A method for treating osteoarthritis in a mammal, said method comprising at least the step of: administering to a mammal in need thereof, an effective amount of a composition comprising a G protein-coupled receptor antagonist compound that: (a) has substantially no agonist activity, and (b) is a cyclic peptide or peptidomimetic compound of General Formula I:



General Formula I

wherein:

A is H, alkyl, aryl, NH_2, NH-alkyl, $N(alkyl)_2$, NH-aryl, NH-acyl, NH-benzoyl, $NHSO_3$, $NHSO_2$-alkyl, $NHSO_2$-aryl, OH, O-alkyl, or O-aryl;

B is an alkyl, aryl, phenyl, benzyl, naphthyl or indole group, or the side chain of a D- or L-amino acid, but is not the side chain of glycine, D-phenylalanine, L-homophenylalanine, L-tryptophan, L-homotryptophan, L-tyrosine, or L-homotyrosine;

C is the side chain of a D-, L- or homo-amino acid, but is not the side chain of isoleucine, phenylalanine, or cyclohexylalanine;

D is the side chain of a neutral D-amino acid, but is not the side chain of glycine or D-alanine, a bulky planar side chain, or a bulky charged side chain;

E is a bulky substituent, but is not the side chain of D-tryptophan, L-*N*-methyltryptophan, L-homophenylalanine, L-2-naphthyl L-tetrahydroisoquinoline, L-cyclohexylalanine, L-leucine, L-fluorenylalanine, or L-histidine;

F is the side chain of L-arginine, L-homoarginine, L-citrulline, or L-canavanine, or a bioisostere thereof; and

$\mathbf{X^1}$ is $-(CH_2)_nNH-$ or $(CH_2)_nS-$, where n is an integer of from 1 to 4; $-(CH_2)_2O-$; $-(CH_2)_3O-$; $-(CH_2)_3-$; $-(CH_2)_4-$; $-CH_2COCHRNH-$; or $-CH_2.CHCOCHRNH-$, where R is the side chain of any common or uncommon amino acid.

18. (New) The method of claim 17, wherein

A is H, alkyl, aryl, NH_2, NH-alkyl, $N(alkyl)_2$, NH-aryl, NH-acyl, NH-benzoyl, $NHSO_3$, $NHSO_2$-alkyl, $NHSO_2$-aryl, OH, O-alkyl, or O-aryl;

B is the side chain of a D- or L-amino acid, but is not the side chain of glycine, D-phenylalanine, L-homophenylalanine, L-tryptophan, L-homotryptophan, L-tyrosine, or L-homotyrosine;

C is the side chain of a D-, L- or homo-amino acid, but is not the side chain of isoleucine, phenylalanine, or cyclohexylalanine;

D is the side chain of a neutral D-amino acid, but is not the side chain of glycine or D-alanine, a bulky planar side chain, or a bulky charged side chain;

E is a bulky substituent, but is not the side chain of D-tryptophan, L-*N*-methyltryptophan, L-homophenylalanine, L-2-naphthyl L-tetrahydroisoquinoline, L-cyclohexylalanine, D-leucine, L-fluorenylalanine, or L-histidine;

F is the side chain of L-arginine, L-homoarginine, L-citrulline, or L-canavanine; and

$\mathbf{X^1}$ is $-(CH_2)_nNH-$ or $(CH_2)_nS-$, where n is an integer from 1 to 4.

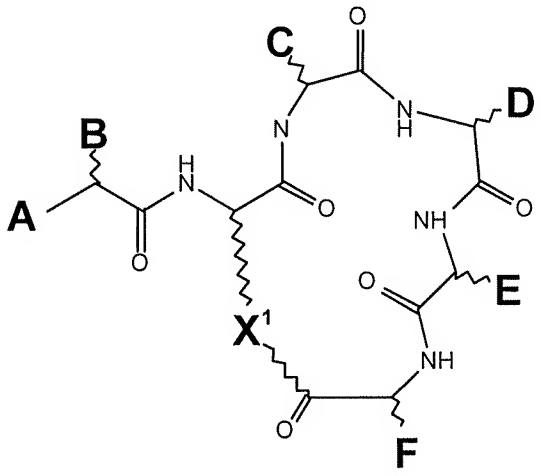
19. (New) The method of claim 18, wherein **A** is NH-acyl; **B** is the side chain of L-phenylalanine; **C** is the side chain of L-proline; **D** is the side chain of D-cyclohexylalanine; **E** is the side chain of L-tryptophan; **F** is the side chain of L-arginine; and $\mathbf{X^1}$ is $-(CH_2)_nNH-$, where n is 3.

20. (New) A method of treatment of osteoarthritis, said method comprising at least the step of administering to a subject in need thereof, an effective amount of a pharmaceutically-acceptable composition that comprises a G protein-coupled receptor inhibitor, wherein said inhibitor:

(a) is an antagonist of a G protein-coupled receptor;

(b) has substantially no agonist activity; and

(c) is a cyclic peptide or peptidomimetic compound of General Formula I:



General Formula I

wherein **A** is NH-acyl; **B** is the side chain of L-phenylalanine; **C** is the side chain of L-proline; **D** is the side chain of D-cyclohexylalanine; **E** is the side chain of L-tryptophan; **F** is the side chain of L-arginine; and $\mathbf{X^1}$ is $-(CH_2)_nNH-$, where *n* is 3.

2. RESPONSE/REMARKS

2.1 STATUS OF THE CLAIMS

Claims 1-15 were pending at the time of the Species Election.

Claims 2-15 have been amended herein.

Claims 16-20 have been added herein.

Claims 1-20 are pending in the case and are ready for initial prosecution on the merits.

2.2 SUPPORT FOR THE CLAIMS

Support for the pending claims can be found throughout the original claims, specification and figures as filed. It will be understood that no new matter is included within any of the present claims. Applicants have made minor amendments to the preamble language of the pending claims to more precisely conform to the traditional language common to U.S. claims' practice. Applicants certify that no new matter has been introduced as a result of these amendments, and further authorize any additional fees necessitated by the present paper to be deducted from Applicants' Representatives' Deposit Account as noted above.

2.3 SPECIES ELECTION

Applicants were asked to elect a single species from the compounds of Formula I (claim 1) for initial prosecution on the merits.

Without acquiescing in any way to the propriety of the species election requirement imposed, and solely to facilitate expeditious examination on the merits of particular embodiments of the invention, Applicants have made the following species election pursuant to 37 C. F. R. § 1.146:

Applicants elect for initial prosecution on the merits the species of General Formula I that is referred to in the present Specification as "AcF-[OPdChaWR]" (and also known as "3D53" and "PMX53" -- see page 10 of the Specification). Compound "PMX53" is also illustrated in co-owned Intl. Pat. Appl. Publ. Nos: PCT/AU02/01427 (referred to therein as "compound 1"), and PCT/AU98/00490 (referred to therein as "compound 17").

Applicants elect a compound of General Formula I, wherein:

A is NH-acyl;

B is the side chain of L-phenylalanine;

C is the side chain of L-proline;

D is the side chain of D-cyclohexylalanine;

E is the side chain of L-tryptophan;

F is the side chain of L-arginine; and

X is $-(CH_2)_nNH-$, where *n* is 3.

These elections are made *without* traverse.

Currently claims 1-2, 6-15, and 17-18 are generic; new claims 16, 19 and 20 read directly on the elected species.

Applicants further reserve the right to rejoin the remaining non-elected species upon allowance of the elected species, and expressly reserve the right to re-file any non-elected inventions in suitable continuing, divisional, or other such applications as may be necessary at such time during the pendancy of the present application.

2.4 CONCLUSION

Applicants believe that the present paper is fully responsive to the outstanding Action, and believes that the pending claims are acceptable under all sections of the Statutes and are in conditions for initial examination on the merits. Should the Examiner have any questions, a telephone call to the undersigned Applicants' representative would be appreciated.

Respectfully submitted,

Mark D. Moore, Ph.D.
Registration No. 42,903

Date: January 23, 2007

HAYNES AND BOONE, LLP
901 Main Street, Suite 3100
Dallas, Texas 75202-3789
Telephone: 713-547-2040
Facsimile: 214-200-0853

H654540

Certificate of Service

I hereby certify that this correspondence is being filed with the U.S. Patent and Trademark Office *via* EFS-Web on January 23, 2007.

Audrey Brown